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=> s TNF?? and (p55 receptor) and (death domain)
'?' TRUNCATION SYMBOL NOT VALID WITHIN 'TNF??'
The truncation symbol ?  may be used only at the end of a search
term.  To specify a variable character within a word use '!', e.g.,
'wom!n' to search for both 'woman' and 'women'.  Enter "HELP
TRUNCATION" at an arrow prompt (=>) for more information.

=> s TNF## and (p55 receptor) and (death domain)
         49284 TNF##
          3364 P55
        557860 RECEPTOR
        511363 RECEPTORS
        664248 RECEPTOR
                 (RECEPTOR OR RECEPTORS)
           507 P55 RECEPTOR
                 (P55(W)RECEPTOR)
        109627 DEATH
          9050 DEATHS
        116151 DEATH
                 (DEATH OR DEATHS)
        225195 DOMAIN
        119717 DOMAINS
        284519 DOMAIN
                 (DOMAIN OR DOMAINS)
          1293 DEATH DOMAIN
                 (DEATH(W)DOMAIN)
L1           8 TNF## AND (P55 RECEPTOR) AND (DEATH DOMAIN)

=> d bib,abs 1-8

L1   ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2000:507750  CAPLUS
DN   133:251050
TI   Activation of ERK1/2 and cPLA2 by the p55 TNF Receptor Occurs
     Independently of FAN
AU   Luschen, Silke; Adam, Dieter; Ussat, Sandra; Kreder, Dirk;
     Schneider-Brachert, Wulf; Kronke, Martin; Adam-Klages, Sabine
CS   Institut fur Immunologie, Christian-Albrechts-Universitat Kiel, Kiel,
     24105, Germany
SO   Biochemical and Biophysical Research Communications (2000), 274(2),
```

506-512
CODEN: BBRCA9; ISSN: 0006-291X
PB Academic Press
DT Journal
LA English
AB The generation of proinflammatory eicosanoids in response to tumor necrosis factor (**TNF**) involves the activation of cytosolic phospholipase A2 (cPLA2), presumably by phosphorylation via extracellular signal-regulated kinases (ERK). Earlier results had suggested that a pathway involving the p55 **TNF** receptor (**TNF**-R55), neutral sphingomyelinase (N-SMase), and c-Raf-1 activates ERK and cPLA2. The authors have previously shown that a cytoplasmic region of **TNF** -R55 distinct from the **death domain** regulates the activation of N-SMase via binding of the adapter protein FAN. Anal. of embryonal fibroblasts from FAN knockout mice revealed that **TNF** -induced activation of both ERK and cPLA2 occurs without involvement of FAN. Furthermore, the authors provide evidence that the **TNF** -dependent activation of ERK and cPLA2 requires the intact **death domain** of **TNF**-R55. Finally, the authors demonstrate that in murine fibroblasts cPLA2 is phosphorylated in response to **TNF** solely by ERK, but not by p38 mitogen-activated protein kinase, suggesting a signaling pathway from **TNF**-R55 via the **death domain** to ERK and cPLA2. (c) 2000 Academic Press.
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:265063 CAPLUS
DN 131:57623
TI Inhibition of receptor internalization by monodansylcadaverine selectively blocks p55 tumor necrosis factor receptor **death domain** signaling
AU Schutze, Stefan; Machleidt, Thomas; Adam, Dieter; Schwandner, Ralf; Wiegmann, Katja; Kruse, Marie-Luise; Heinrich, Michael; Wickel, Marc; Kronke, Martin
CS Institute of Immunology, University of Kiel, Kiel, 24105, Germany
SO Journal of Biological Chemistry (1999), 274(15), 10203-10212
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB The 55-kDa receptor for tumor necrosis factor (TR55) triggers multiple signaling cascades initiated by adapter proteins like TRADD and FAN. By use of the primary amine monodansylcadaverine (MDC), the authors addressed the functional role of tumor necrosis factor (**TNF**) receptor internalization for intracellular signal distribution. They show that MDC does not prevent the interaction of the p55 **TNF** receptor (TR55) with FAN and TRADD. Furthermore, the activation of plasma membrane-associated neutral sphingomyelinase activation as well as the stimulation of proline-directed protein kinases were not affected in MDC-treated cells. In contrast, activation of signaling enzymes that are linked to the "**death domain**" of TR55, like acid sphingomyelinase and c-Jun-N-terminal protein kinase as well as **TNF** signaling of apoptosis in U937 and L929 cells, are blocked in the presence of MDC. The results of the authors' study suggest a role of TR55 internalization for the activation of select TR55 **death domain** signaling pathways including those leading to apoptosis.
RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:360447 CAPLUS
DN 129:107598
TI Distinct adapter proteins mediate acid versus neutral sphingomyelinase

activation through the **p55 receptor** for tumor necrosis factor

AU Adam-Klages, Sabine; Schwandner, Ralf; Adam, Dieter; Kreder, Dirk; Bernardo, Katussevani; Kronke, Martin

CS Institut fur Immunologie, Christian-Albrechts-Universitat Kiel, Kiel, 24105, Germany

SO Journal of Leukocyte Biology (1998), 63(6), 678-682
CODEN: JLBIE7; ISSN: 0741-5400

PB Federation of American Societies for Experimental Biology

DT Journal; General Review

LA English

AB A review with 48 refs. The activation of 2 distinct sphingomyelinases (SMase) via tumor necrosis factor receptor p55 is mediated by different adapter proteins that interact with sep. cytoplasmic domains. The **death domain**-associated proteins TRADD and FADD mediate A-SMase activation, but also cell death. How the ceramide generated by A-SMase is involved in the induction of apoptosis is not fully understood. It appears, however, likely that ceramide might serve as a cofactor in the induction of apoptosis by tumor necrosis factor. The activation of N-SMase is mediated by the novel WD-repeat protein FAN. Because N-SMase signaling has been linked to the activation of the pro-inflammatory cPLA2, FAN might represent a valuable target for the development of anti-inflammatory tumor necrosis factor antagonists.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:428113 CAPLUS

DN 127:160369

TI Induced expression of trimerized intracellular domains of the human tumor necrosis factor (**TNF**) **p55 receptor** elicits **TNF** effects

AU Vandevoorde, Veronique; Haegeman, Guy; Fiers, Walter

CS Laboratory of Molecular Biology, Flanders Interuniversity Institute for Biotechnology and University of Ghent, Ghent, B-9000, Belg.

SO Journal of Cell Biology (1997), 137(7), 1627-1638
CODEN: JCLBA3; ISSN: 0021-9525

PB Rockefeller University Press

DT Journal

LA English

AB The various biol. activities of tumor necrosis factor (**TNF**) are mediated by 2 receptors, one of 55 kDa (**TNF**-R55) and one of 75 kDa (**TNF**-R75). Although the phenotypic and mol. responses elicited by **TNF** in different cell types are fairly well characterized, the signaling pathways leading to them are so far only partly understood. To further unravel these processes, the authors focused on **TNF**-R55, which is responsible for mediating most of the known **TNF** effects. Since several studies have demonstrated the importance of receptor clustering and consequently of close association of the intracellular domains for signaling, the authors addressed the question of whether clustering of the intra-cellular domains of **TNF**-R55 (**TNF**-R55i) needs to occur in structural association with the inner side of the cell membrane, where many signaling mediators are known to reside. Therefore, the authors investigated whether induced intracellular clustering of only **TNF**-R55i would be sufficient to initiate and generate a full **TNF** response, without the need for a full-length receptor mol. or a transmembrane region. The results provide clear evidence that inducible forced trimerization of either **TNF**-R55i or only the **death domain** elicits an efficient **TNF** response, comprising activation of the nuclear factor kB, induction of interleukin-6, and cell killing.

L1 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:847321 CAPLUS

DN 124:53337
TI Cloning of the cDNA encoding the porcine p55 tumor necrosis factor receptor
AU Suter, B.; Pauli, U.
CS Institute of Veterinary Virology, University of Bern, Laenggass-Str. 122, CH-3012, Bern, Switz.
SO Gene (1995), 163(2), 263-6
CODEN: GENED6; ISSN: 0378-1119
PB Elsevier
DT Journal
LA English
AB RT-PCR was used to clone the porcine p55TNFR cDNA, encoding the 55-kDa tumor necrosis factor receptor (**TNFR**), encompassing the entire coding region and most of the 3' untranslated region. PCR was performed using total cellular RNA of porcine kidney cell line 15 [PK(15)] and primers for the human p55TNFR. Since the length of the entire fragment was >2000 bp, 2 amplified subfragments were fused with the help of a restriction endonuclease. The entire fragment was cloned and its amino acid (aa) sequence was compared to the human, rat, and mouse p55TNFR. This comparison revealed identities of 79, 71, and 72%, resp. The highest identities of 90, 80, and 85% were detected in the so called " **death domain**" for the human, rat, and mouse sequences, resp. This domain is crucial for the cytotoxic signal transduction of p55TNFR.

L1 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:655578 CAPLUS
DN 123:333024
TI A protein related to a proteasomal subunit binds to the intracellular domain of the p55 **TNF** receptor upstream to its '**death domain**'
AU Boldin, Mark P.; Mett, Igor L.; Wallach, David
CS Department of Membrane Research and Biophysics, The Weizmann Institute of Science, Rehovot, 76100, Israel
SO FEBS Letters (1995), 367(1), 39-44
CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier
DT Journal
LA English
AB A novel protein that binds specifically to the intracellular domain of the p55 tumor necrosis factor (**TNF**) receptor was cloned by two-hybrid screening of a HeLa cell cDNA library. Data bank searches revealed high sequence similarity of the protein (55.11) to yeast, nematode and plant proteins, whose functions are yet unknown. Significant similarity was also found between 55.11 and SEN3, the yeast equivalent of the p112 subunit of the 26S proteasome. Deletion anal. showed that the protein binds to the **p55 receptor** upstream to the region involved in induction of cell death.

L1 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:311512 CAPLUS
DN 122:79097
TI Self-association of the "**death domains**" of the p55 tumor necrosis factor (**TNF**) receptor and Fas/APO1 prompts signaling for **TNF** and Fas/APO1 effects
AU Boldin, Mark P.; Mett, Igor L.; Varfolomeev, Eugene E.; Chumakov, Irina; Shemer-Avni, Yonat; Camonis, Jacques H.; Wallach, David
CS Dep. Membr. Res. Biophys., Weizmann Inst. Sci., Rehovot, 76100, Israel
SO Journal of Biological Chemistry (1995), 270(1), 387-91
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Signaling by the p55 tumor necrosis factor (**TNF**) receptor and by

the structurally related receptor Fas/APO1 is initiated by receptor clustering. Data presented here and in other recent studies (Wallach, D., et al., 1994; Song, H. Y., et al., 1994) indicate that part of that region within the intracellular domains of the two receptors that is involved in signaling for cell death, as well as for some other effects (the "**death domain**"), specifically self-assocs. The authors demonstrate also the expected functional consequence of this association; a mere increase in p55 **TNF** receptor expression, or the expression just of its intracellular domain, is shown to trigger signaling for cytotoxicity as well as for interleukin 8 gene induction, while expression of the intracellular domain of Fas/APO1 potentiates the cytotoxicity of co-expressed p55 **TNF** receptor. Thus, the p55 **TNF** and Fas/APO1 receptors play active roles in their own clustering and the existence is suggested of cellular mechanisms that restrict the self-association of these receptors, thus preventing constitutive signaling.

L1 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:189309 CAPLUS
DN 120:189309
TI A novel domain within the 55 kDa **TNF** receptor signals cell death
AU Tartaglia, Louis A.; Ayres, T. Merrill; Wong, Grace H. W.; Goeddel, David V.
CS Dep. Mol. Biol., Genentech, Inc., South San Francisco, CA, 94080, USA
SO Cell (Cambridge, MA, United States) (1993), 74(5), 845-53
CODEN: CELLB5; ISSN: 0092-8674
DT Journal
LA English
AB Deletion mutagenesis of the intracellular region of the 55 kDa **TNF** receptor (**TNF**-R1) identified an .apprx.80 amino acid domain near the C-terminus responsible for signaling cytotoxicity. This domain shows weak homol. with the intracellular domain of Fas antigen, a transmembrane polypeptide that can also initiate a signal for cytotoxicity. Alanine-scanning mutagenesis of **TNF**-R1 confirmed that many of the amino acids conserved with Fas antigen are critical for the cytotoxic signal. This region of **TNF**-R1-Fas homol. is therefore likely to define a novel domain (**death domain**) that signals programmed cell death. Mutations within the **death domain** of **TNF**-R1 also disrupted its ability to signal anti-viral activity and nitric oxide (NO) synthase induction. In addition, large deletions in the membrane-proximal half of the intracellular domain did not block signaling of cytotoxicity or anti-viral activity but did block induction of NO synthase.